AMENDMENT UNDER 37 C.F.R. § 1.111 Attorney Docket No.: Q59123

U.S. Application No.: 09/530,807

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the

application:

LISTING OF CLAIMS:

45. (currently amended): A method for the treatment of diseases of the central nervous

system (excluding those involving CNS depressant action), the cardiovascular system (excluding

hypertension), the kidney, or diseases associated with abnormal adrenal gland secretions, or for

the treatment of hyperglycaemia or peptic ulcer, which comprises administering an effective

amount of a compound of formula II:

wherein W is optionally substituted aryl; optionally substituted C<sub>5</sub>-C<sub>7</sub> cycloalkyl; -CHR<sup>1</sup>R<sup>2</sup>

where R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl,

optionally substituted  $C_3$ - $C_7$  cycloalkyl and optionally substituted arylor  $R^1$  and  $R^2$  are linked to

form an optionally substituted C<sub>5</sub>-C<sub>7</sub> cycloalkyl; OR' where R' is optionally substituted aryl;

optionally substituted C3-C7-cycloalkyl; or optionally substituted C4-C6-alkyl; provided that R4

2

and R<sup>2</sup> are not both hydrogen;

Z is imino, C<sub>1</sub>-C<sub>2</sub>-alkylene, -CH<sub>2</sub>NH-or-CH<sub>2</sub>CH<sub>2</sub>NH-;

AMENDMENT UNDER 37 C.F.R. § 1.111

U.S. Application No.: 09/530,807

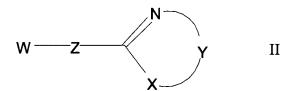
Attorney Docket No.: Q59123

X is O-or S; and

Y is optionally substituted C<sub>2</sub>-C<sub>3</sub> alkylene; provided that W is not OR' when Z is imino or -CH<sub>2</sub>NH;

or a pharmaceutically acceptable salt or ester thereof.

- 46. (currently amended): The method according to claim 45 wherein the disease is a disease of the central nervous system selected from the group consisting of dementia, mood disturbances, degenerative conditions and neurodegenerative diseases.
- 47. (currently amended): A method for the treatment of glaucoma comprising administering an effective amount of a compound of formula II



wherein W is optionally substituted aryl; optionally substituted  $C_5$   $C_7$  cycloalkyl; -CHR<sup>1</sup>R<sup>2</sup> where R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl and optionally substituted aryl or R<sup>1</sup> and R<sup>2</sup> are linked to form an optionally substituted C<sub>5</sub>-C<sub>7</sub> cycloalkyl; OR' where R' is optionally substituted aryl;

AMENDMENT UNDER 37 C.F.R. § 1.111

U.S. Application No.: 09/530,807

optionally substituted C<sub>3</sub>-C<sub>2</sub>-cycloalkyl; or optionally substituted C<sub>4</sub>-C<sub>6</sub>-alkyl; provided that R<sup>4</sup> and R<sup>2</sup> are not both hydrogen;

Z is imino, C<sub>1</sub>-C<sub>2</sub>-alkylene, CH<sub>2</sub>NH or CH<sub>2</sub>CH<sub>2</sub>NH;

X is O-or-S; and

Y is optionally substituted  $C_2$ - $C_3$  alkylene; provided that W is not OR' when Z is imino or  $-CH_2NH$ ; and

with the further provisos that

- a) when Y is CH<sub>2</sub>CH<sub>2</sub>, X is O and Z is imino then
  - (i) if W is CHR<sup>1</sup>R<sup>2</sup> and R<sup>1</sup> is H then R<sup>2</sup> is not selected from phenyl; phenyl substituted with methoxy, Br, Cl, F or trifluoromethyl; 3-nitrophenyl; 3- or 4-methylphenyl; 2- or 4-bromomethyl phenyl; 2- or 4-chloromethylphenyl; or 2,3- or 2,6-dimethylphenyl; and
  - (ii) if W is CHR<sup>1</sup>R<sup>2</sup> and R<sup>1</sup> is CH<sub>3</sub> or cyclopropyl then R<sup>2</sup> is not phenyl or phenyl substituted with alkyl, halomethyl, fluoro or trifluoromethyl; and
- b) when Y is  $(CH_2)_{2-4}$ , X is O-or-S, Z is imino and W is  $CHR^1R^2$ , then
  - (i) if R<sup>1</sup> is CF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub> or CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub> then R<sup>2</sup> is not alkyl, optionally substituted cycloalkyl or optionally substituted aryl, and
  - (ii) if R<sup>1</sup> is optionally substituted cyclopropyl, R<sup>2</sup> is not H, alkyl or optionally substituted cyclopropyl;

AMENDMENT UNDER 37 C.F.R. § 1.111

U.S. Application No.: 09/530,807

Attorney Docket No.: Q59123

or a pharmaceutically acceptable ester or salt thereof, to a subject in need thereof.

48. (currently amended): A method for the treatment of diseases of the central nervous system, cardiovascular system, or the kidney, or for the treatment of diseases associated with abnormal adrenal gland secretions, or in the treatment of hyperglycaemia, glaucoma, peptic ulcer or to produce analgesia which comprises administering an effective amount of a compound of formula II

wherein W is optionally substituted aryl; optionally substituted  $C_5$   $C_7$  cycloalkyl;  $-CHR^1R^2$  where  $R^1$  and  $R^2$  are independently selected from hydrogen, optionally substituted  $C_1$ - $C_6$  alkyl, optionally substituted  $C_3$ - $C_7$  cycloalkyl and optionally substituted aryl or  $R^1$  and  $R^2$  are linked to form an optionally substituted  $C_5$ - $C_7$  cycloalkyl; OR' where R' is optionally substituted aryl; optionally substituted  $C_3$   $C_7$  cycloalkyl; or optionally substituted  $C_4$   $C_6$  alkyl; provided that  $R^4$  and  $R^2$  are not both hydrogen;

Z is imino, C<sub>1</sub>-C<sub>2</sub>-alkylene, CH<sub>2</sub>NH- or -CH<sub>2</sub>CH<sub>2</sub>NH-;

X is O-or S; and

Y is optionally substituted  $C_2$ - $C_3$  alkylene; provided that W is not OR' when Z is imino or  $-CH_2NH$ ; and

AMENDMENT UNDER 37 C.F.R. § 1.111 U.S. Application No.: 09/530,807

with the further provisos that

- a) when Y is CH<sub>2</sub>CH<sub>2</sub>, X is O and Z is imino then
  - (i) W is not unsubstituted or 2-mono-, 2,2-di, 2,5-di, 2,6-di or 2,4,6-tri C<sub>1-3</sub> alkyl substituted cyclohexyl or 2-mono- or 2,5,-di C<sub>1-3</sub> alkyl substituted cycloheptyl; and
  - (ii) if W is CHR<sup>1</sup>R<sup>2</sup> and R<sup>1</sup> is H then R<sup>2</sup> is not selected from phenyl; phenyl substituted with methoxy, Br. C1, F or trifluoromethyl; 3-nitrophenyl; 3- or 4-methylphenyl; 2- or 4-bromomethylphenyl; 2- or 4-chloromethylphenyl; or 2,3- or 2,6 dimethylphenyl; and
  - (iii) if W is CHR<sup>1</sup>R<sup>2</sup> and R<sup>1</sup> is CH<sub>3</sub> or cyclopropyl then R<sup>1</sup> is not phenyl or phenyl substituted with alkyl, halomethyl, fluoro or trifluoromethyl; and
- b) when Y is  $(CH_2)_{2-4}$ , X is O-or-S, Z is imino and W is  $CHR^1R^2$ , then
  - (i) if R<sup>1</sup> is CF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub> or CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub> then R<sup>2</sup> is not alkyl, optionally substituted cycloalkyl or optionally substituted aryl, and
  - (ii) if R<sup>1</sup> is optionally substituted cyclopropyl, R<sup>2</sup> is not H, alkyl or optionally substituted cyclopropyl;

or a pharmaceutically acceptable ester or salt thereof, to a subject in need thereof.

49. (previously presented): The method according to claim 46, wherein the disease is a degenerative condition selected from the group consisting of stroke, aging, ischemia, and CNS trauma.

AMENDMENT UNDER 37 C.F.R. § 1.111 U.S. Application No.: 09/530,807

50. (previously presented): The method according to claim 46, wherein the disease is a neurodegenerative disease selected from the group consisting of Alzheimer's disease and Parkinson's disease.

(currently amended): The method according to claim 45, 47 or 48, wherein W is 51. aryl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> haloalkyl, halogen, C<sub>2</sub> C<sub>6</sub> cycloalkyl, aryl, C<sub>2</sub> C<sub>6</sub> alkenyl, C<sub>1</sub> C<sub>6</sub> alkynyl or aryloxy); C<sub>5</sub> C<sub>6</sub> cycloalkyl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub>-haloalkyl,  $\frac{\text{halogen, } C_3\text{-}C_6\text{-}\text{cycloalkyl, aryl, } C_2\text{-}C_6\text{-}\text{alkenyl, } C_2\text{-}C_6\text{-}\text{alkynyl or aryloxy); -}\text{CHR}^1R^2\text{ where }R^1$ and R<sup>2</sup> are independently selected from hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> haloalkyl, halogen, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl or aryloxy), C<sub>3</sub>-C<sub>6</sub> cycloalkyl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> haloalkyl, halogen, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C2-C6 alkynyl or aryloxy) and aryl (optionally substituted with hydroxy, C1-C6 alkyl, C1-C<sub>6</sub> alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub> haloalkyl, halogen, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl or aryloxy); OR' where R' is aryl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, NO<sub>2</sub>, NH<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, halogen, C<sub>2</sub>-C<sub>6</sub>-cycloalkyl, aryl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl or aryloxy); C3-C6-cycloalkyl (optionally substituted with hydroxy, C1-C6-alkyl, C1-C6 alkoxy, NO2, NH2, C1-C6 haloalkyl, halogen, C3-C6 cycloalkyl, aryl, C2-C6 alkenyl, C2-C6 alkynyl or aryloxy); or C<sub>1</sub>-C<sub>6</sub> alkyl (optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, NO2, NH2, C1-C6 haloalkyl, halogen, C2-C6 cycloalkyl, aryl, C2-C6 alkenyl, C2-C6 alkynyl or aryloxy).

AMENDMENT UNDER 37 C.F.R. § 1.111 Attorney Docket No.: Q59123

U.S. Application No.: 09/530,807

52. (currently amended): The method according to claim 45, 47 or 48, wherein W is phenyl, cyclohexyl or naphthyl, each of which may be optionally substituted with one to three substituents selected from hydroxy, methoxy, ethoxy, benzyloxy, NO<sub>2</sub>, NH<sub>2</sub>, halogen, methyl and ethyl; or CHR<sup>1</sup>R<sup>2</sup> where R<sup>1</sup> and R<sup>2</sup> are independently selected from phenyl, naphthyl, cyclohexyl, cyclopentyl, cyclopropyl, methyl, ethyl, propyl and butyl, each of which may be optionally substituted with hydroxy, methoxy, ethoxy, benzyloxy, NO<sub>2</sub>, NH<sub>2</sub>, halogen, methyl and ethyl.

- 53. (canceled).
- 54. (previously presented): The method according to claim 45, 47 or 48, wherein Y is  $C_2$ - $C_3$  alkylene optionally substituted with  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl,  $C_1$ - $C_6$  alkyloxycarbonyl, or with two substituents which join together to form a 5-6 membered carbocyclic or heterocyclic ring.
- 55. (previously presented): The method according to claim 54, wherein Y is unsubstituted  $C_2$ - $C_4$  alkylene.
- 56. (previously presented): The method according to claim 54, wherein Y is ethylene.
- 57. (currently amended): The method according to claim 45, 47 or 48, wherein the compound of formula II is a compound of formula III:

## AMENDMENT UNDER 37 C.F.R. § 1.111 U.S. Application No.: 09/530,807

$$\mathbb{R}^{6}$$
 $\mathbb{R}^{5}$ 
 $\mathbb{R}^{4}$ 
 $\mathbb{R}^{6}$ 
 $\mathbb{R}^{7}$ 
 $\mathbb{R}^{8}$ 

wherein  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from hydrogen, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $NO_2$ ,  $NH_2$ ,  $C_1$ - $C_6$  haloalkyl, halogen,  $C_3$ - $C_6$  cycloalkyl, aryl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl and aryloxy;

Z is imino, C<sub>1</sub>-C<sub>2</sub> alkylene, or -CH<sub>2</sub>CH<sub>2</sub>NH-;

R<sup>7</sup> and R<sup>8</sup> are independently selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkanoyloxy and C<sub>1</sub>-C<sub>6</sub> alkyloxycarbonyl, or R<sup>7</sup> and R<sup>8</sup> may together form a 5 or 6 membered aromatic or non-aromatic carbocyclic or heterocyclic ring;

a compound of formula IV:

$$\mathbb{R}^3$$
  $\mathbb{R}^7$   $\mathbb{R}^7$   $\mathbb{R}^8$ 

where  $R^3$ ,  $R^4$ ,  $R^7$ ,  $R^8$  and Z are as defined in relation to formula III;

a compound of formula V:

## AMENDMENT UNDER 37 C.F.R. § 1.111 Attorney Docket No.: Q59123

U.S. Application No.: 09/530,807

where  $R^3$ ,  $R^4$ ,  $R^7$  and Z are as defined in relation to formula III, and  $R^9$  is  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

a compound of formula VI:

where  $R^7$ ,  $R^8$  and Z are as defined in relation to formula III and  $R^{10}$  and  $R^{11}$  are independently selected from hydrogen,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $NO_2$ ,  $NH_2$ ,  $C_1$ - $C_6$  haloalkyl, halogen,  $C_3$ - $C_6$  cycloalkyl, aryl,  $C_3$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl and aryloxy; or

a compound of formula VII:

where  $R^7$ ,  $R^8$  and Z are as defined in relation to formula III and  $R^{12}$  is hydrogen optionally substituted  $C_1$ - $C_6$  alkyl, optionally substituted  $C_3$ - $C_7$  cycloalkyl or optionally substituted aryl; a

AMÉNDMENT UNDER 37 C.F.R. § 1.111

U.S. Application No.: 09/530,807

Attorney Docket No.: Q59123

## compound of formula VIII:

where φ is optionally substituted aryl and R<sup>7</sup>, R<sup>8</sup> and Z are defined in relation to formula III; a compound of formula IX:

where  $R^7$ ,  $R^8$  and Z and  $\phi$  are as defined in relation to formula VIII; or a compound of formula X:

$$\mathbb{R}^{12}$$
 $\mathbb{R}^{7}$ 
 $\mathbb{R}^{7}$ 
 $\mathbb{R}^{8}$ 

where  $R^7$ ,  $R^8$ ,  $R^{12}$  and Z are as defined in relation to formula VII and  $\phi$  is as defined in relation to formula IX.